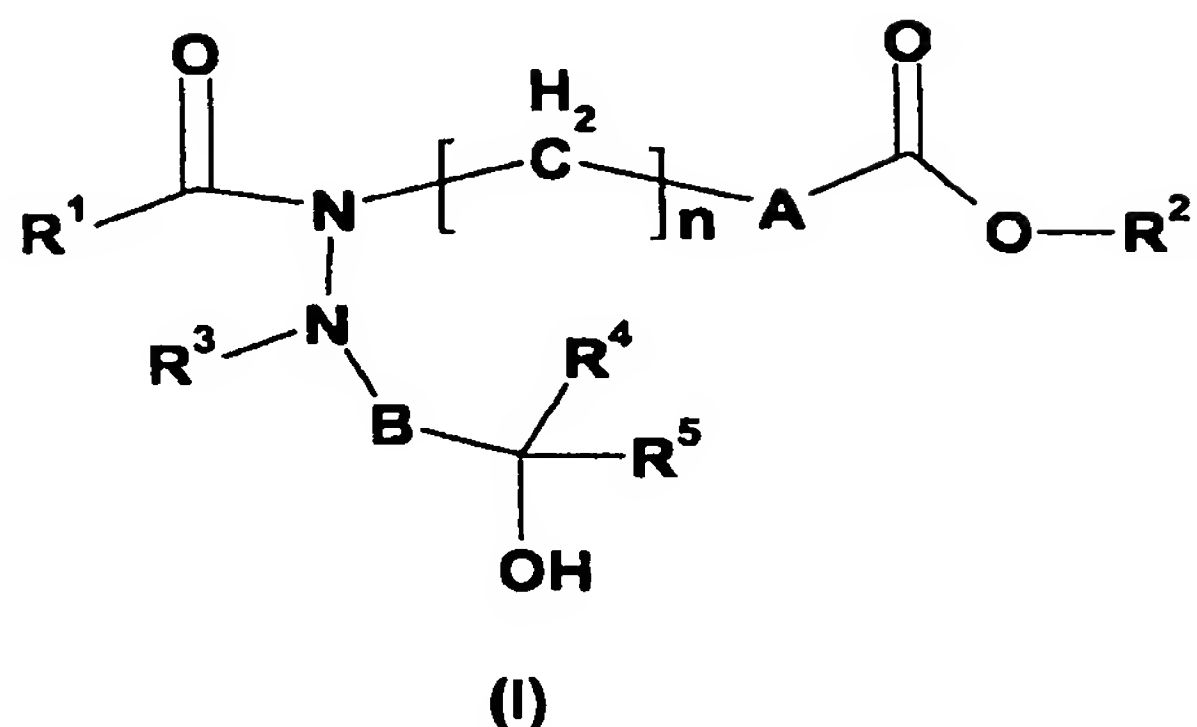


Claims

1. A hydrazide derivative of Formula (I):



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as well as its geometrical isomers, its optically active forms as enantiomers, diastereomers and mixtures of these, as well as salts thereof, wherein:

A is selected from C₃-C₈ cycloalkyl, heterocycloalkyl, aryl and heteroaryl;

B is selected from C₁-C₆ alkylene, C₂-C₆ alkenylene, and C₂-C₆ alkynylene;

10 R¹ is selected from H, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, heterocycloalkyl, aryl C₁-C₆ alkyl, heteroaryl C₁-C₆ alkyl, aryl and heteroaryl;

R² and R³ are independently selected from H, C₁-C₆ alkyl, C₂-C₆ alkenyl and C₂-C₆ alkynyl.

R⁴ is selected from hydrogen and C₁-C₆ alkyl;

15 R⁵ is selected from hydrogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ heteroalkyl, C₃-C₈ cycloalkyl, C₃-C₈ cycloalkyl C₁-C₆ alkyl, aryl C₁-C₆ alkyl, heteroaryl C₁-C₆ alkyl, aryl and heteroaryl;

n is an integer selected from 1, 2, 3, 4, 5 and 6.

2. A hydrazide derivative of claim 1 wherein A is selected from aryl and heteroaryl.

- 20 3. A hydrazide derivative according claims 1 or 2 wherein A is phenyl.

4. A hydrazide derivative according to any of the preceding claims wherein B is ethylene.
5. A hydrazide derivative according to any of the preceding claims wherein R¹ is C₁-C₆ alkyl.
- 5 6. A hydrazide derivative according to any of the preceding claims wherein R² is H.
7. A hydrazide derivative according to any of the preceding claims wherein R³ is selected from H and methyl.
8. A hydrazide derivative according to any of the preceding claims wherein R³ H.
9. A hydrazide derivative according to any of the preceding claims wherein R⁴ is H.
- 10 10. A hydrazide according to any of the preceding claims wherein n is 2.
11. A hydrazide derivative according to any of the preceding claims wherein A is phenyl; B is ethylenyl; R¹ is C₁-C₆ alkyl; R² and R⁴ are H; R³ is selected from H and methyl; and n is 2.
12. A hydrazide derivative according to any of the preceding claims wherein R⁵ is
15 selected from H, C₁-C₆ alkyl and C₃-C₆ cycloalkyl
13. A hydrazide derivative according to any of the preceding claims wherein R⁵ is aryl C₁-C₆ alkyl.
14. A hydrazide derivative according to any of the preceding claims wherein R⁵ is heteroaryl C₁-C₆ alkyl.
- 20 15. A hydrazide derivative according to any of the preceding claims wherein R⁵ is C₃-C₈ cycloalkyl.
16. A hydrazide derivative according to any of the preceding claims selected from the following group:

- 4-(2-{1-acetyl-2-[4-(3-chlorophenyl)-3-hydroxybutyl]hydrazino}ethyl)benzoic acid;
 4-(2-{1-acetyl-2-[3-hydroxy-4-(3-iodophenyl)butyl]hydrazino}ethyl)benzoic acid;
 4-(2-{1-acetyl-2-[4-(3-bromophenyl)-3-hydroxybutyl]hydrazino}ethyl)benzoic acid;
 4-(2-{1-acetyl-2-[4-(1,1'-biphenyl-3-yl)-3-hydroxybutyl]hydrazino}ethyl)benzoic
 5 acid;
 4-[2-(1-acetyl-2-{3-hydroxy-4-[3-(phenylethynyl)phenyl]butyl}hydrazino)ethyl]
 benzoic acid;
 4-{2-[1-acetyl-2-(3-hydroxy-4-phenylbutyl)hydrazino]ethyl}benzoic acid;
 4-(2-{1-acetyl-2-[4-(4-chlorophenyl)-3-hydroxybutyl]hydrazino}ethyl)benzoic acid;
 10 4-(2-{1-acetyl-2-[4-(4-fluorophenyl)-3-hydroxybutyl]hydrazino}ethyl)benzoic acid;
 4-(2-{1-acetyl-2-[4-(3-ethynylphenyl)-3-hydroxybutyl]hydrazino}ethyl)benzoic acid;
 4-(2-{1-acetyl-2-[4-(3-fluorophenyl)-3-hydroxybutyl]hydrazino}ethyl)benzoic acid;
 4-[2-(1-acetyl-2-{3-hydroxy-4-[4-(phenylethynyl)phenyl]butyl}hydrazino)ethyl]
 benzoic acid;
 15 4-{2-[1-acetyl-2-(3-hydroxy-4-thien-2-ylbutyl)hydrazino]ethyl}benzoic acid;
 4-[2-(1-acetyl-2-{4-[3-(cyclopropylethynyl)phenyl]-3-hydroxybutyl}hydrazino)ethyl]
 benzoic acid;
 4-[2-(2-{3-hydroxy-4-[3-(trifluoromethyl)phenyl]butyl}-1-isobutyrylhydrazino)ethyl]
 benzoic acid;
 20 4-[2-(2-{3-hydroxy-4-[3-(trifluoromethyl)phenyl]butyl}-1-propionylhydrazino)ethyl]
 benzoic acid;
 4-[2-(1-acetyl-2-{3-hydroxy-4-[3-(trifluoromethyl)phenyl]butyl}hydrazino)ethyl]
 benzoic acid;
 4-{2-[1-acetyl-2-(3-cyclohexyl-3-hydroxypropyl)hydrazino]ethyl}benzoic acid; or a
 25 pharmaceutically acceptable salt of any of said compounds.

17. A hydrazide derivative selected from the following group:

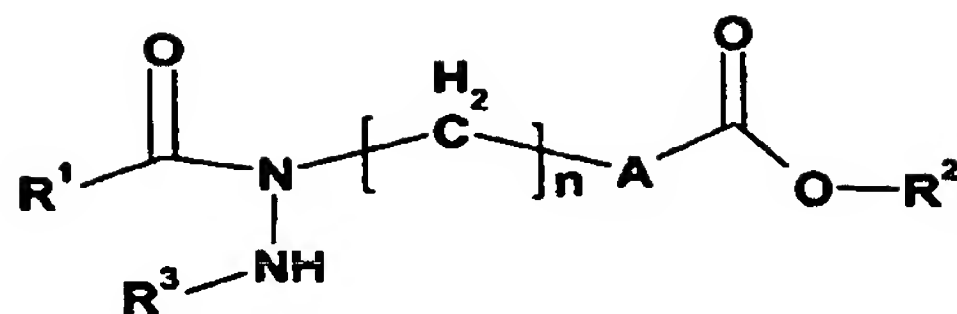
- 4-{2-[1-acetyl-2-(3-hydroxyoctyl)hydrazino]ethyl}benzoic acid;
 4-{2-[1-acetyl-2-(3-hydroxyoctyl)-2-methylhydrazino]ethyl}benzoic acid;
 4-{2-[1-acetyl-2-(3-hydroxybutyl)hydrazino]ethyl}benzoic acid;

or a pharmaceutically acceptable salt of any of said compounds.

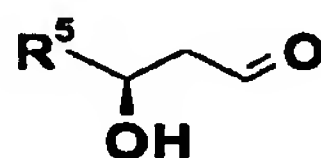
18. A hydrazide derivative according to any of the preceding claims for use as a medicament.
19. A method for treating a disease or disorder associated with prostaglandins,
5 comprising administering to a mammal suffering from or susceptible to such a disease or disorder an effective amount of a compound of any one of claims 1 through 17.
20. A method for treating a mammal is suffering from or susceptible to pre-term labor,
10 dysmenorrhea, asthma, hypertension, undesired blood clotting, pre-eclampsia, eclampsia, an eosinophil disorder, undesired bone loss, renal dysfunction, an immune deficiency disorder, dry eye, ichthyosis, elevated intra-ocular pressure, a gastric ulcer, fertility disorders, sexual dysfunction and inflammatory disorders comprising administering to the mammal an effective amount of a compound of any one of claims 1 through 17.
- 15 21. A method according to claims 19 or 20 wherein the mammal is suffering from or susceptible undesired muscle contraction.
22. A method according to claim 19 wherein the mammal is suffering from or susceptible to pre-term labor.
23. A method according to claims 19 or 20 wherein the mammal is suffering from or
20 susceptible to a respiratory disease selected from asthma, chronic obstructive respiratory disease and emphysema.
24. A method of claims 19 or 20 wherein the mammal is suffering from or susceptible to hypertension.
25. A method of claims 19 or 20 wherein the mammal is suffering from or susceptible to
25 bone loss.

26. A method of claims 19 or 20 wherein the mammal is suffering from or susceptible ovulatory disorders.
27. A method of claims 19 or 20 wherein the mammal is suffering from or susceptible erectile dysfunction.
- 5 28. Use of a compound of any one of claims 1 through 17 for the preparation of a medicament to treat a disease or disorder associated with prostaglandin.
29. Use of a compound of any one of claims 1 through 17 for the preparation of a medicament to treat a disorder or a disease selected from preterm labor, dysmenorrhea, asthma, chronic obstructive respiratory disease, emphysema,
10 hypertension, undesired blood clotting, preeclampsia, eclampsia, an eosinophil disorder, undesired bone loss, renal dysfunction, an immune deficiency disorder, dry eye, ichthyosis, elevated intraocular pressure, gastric ulcers, fertility disorders, sexual dysfunction and inflammatory disorders.
30. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and
15 one or more compounds of any one of claims 1 through 17.
31. A pharmaceutical composition of claim 30 wherein the compound is packaged together with instructions for use of the compound to treat a disorder or a disease selected from preterm labor, dysmenorrhea, asthma, hypertension, undesired blood clotting, a destructive bone disease or disorder, preeclampsia or eclampsia, an
20 eosinophil disorder, renal dysfunction an immune deficiency disorder, dry eye, ichthyosis, elevated intraocular pressure and gastric ulcers.
32. A process for the preparation of a hydrazide derivative according to any of claims 1 to 17, comprising the step of a reductive amination of a hydrazide of Formula II with a compound of Formula III in presence of a reducing agent:

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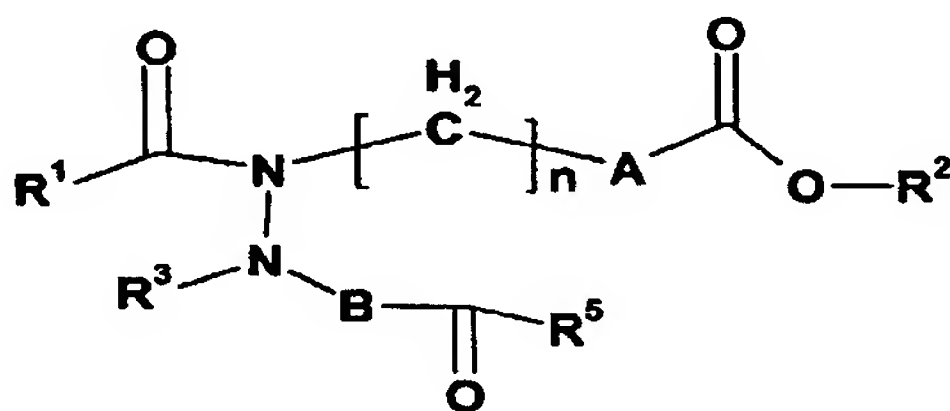
(II)



(III)

wherein A, R¹, R², R³ and n are as defined above; R⁵ is -CH₂-R⁶ wherein R⁶ is selected from C₁-C₅ alkyl, C₂-C₅ alkenyl, C₂-C₅ alkynyl, C₁-C₅ heteroalkyl, C₁-C₅ alkyl C₁-C₅ alkyl, aryl C₁-C₅ alkyl and heteroaryl C₁-C₅ alkyl.

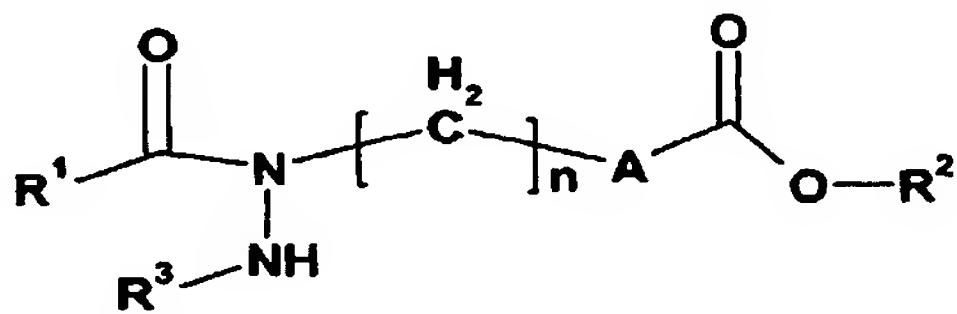
33. A process for the preparation of a hydrazide derivative according to any of claims 1 to 13, comprising the step of a reduction of a compound of Formula IV:



(IV)

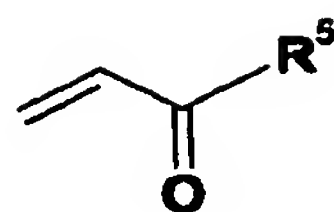
wherein A, B, R¹, R², R³, R⁵ and n are as defined above.

34. A process of claim 29, further comprising the step of an addition of compound of Formula V to a compound of Formula II through a Michael addition:



(III)

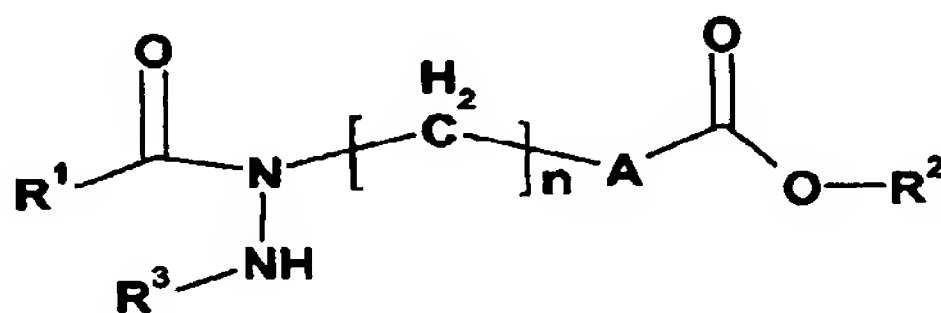
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(V)

wherein A, B, R¹, R², R³ and R⁵ are as defined above; R⁴ is H.

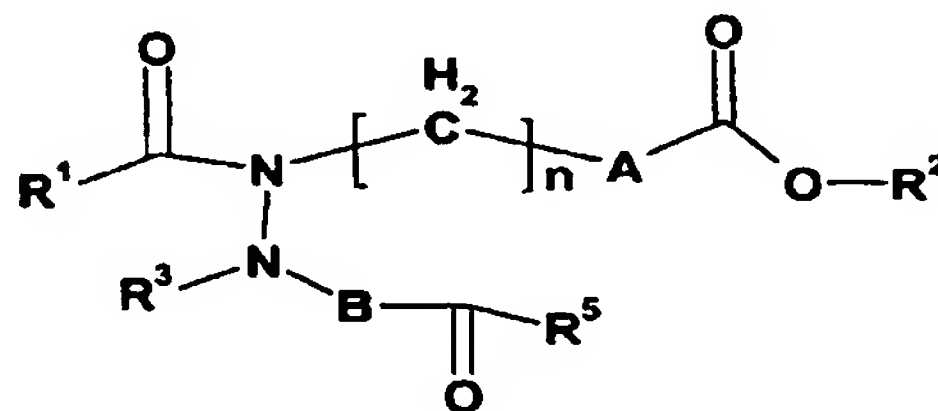
35. A process according to claims 32 to 34, further comprising the step of saponification of the resulting compound of Formula I wherein R¹ is not H into a compound of Formula I wherein R² is H.
36. A process according to claims 32 to 35 wherein A is phenyl.
37. A compound of Formula II:



(II)

- as well as its geometrical isomers, its optically active forms as enantiomers, diastereomers and mixtures of these, as well as salts thereof, wherein A, R¹, R², R³ and n are as defined above.

38. A compound of Formula IV:



(IV)

as well as its geometrical isomers, its optically active forms as enantiomers, diastereomers and mixtures of these, as well as salts thereof, wherein A, R¹, R², R³, R⁵ and n are as defined above.